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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/990,909	11/16/2001	Joan M. Fallon	8016-5	3427

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EXAMINER	
LUCAS, ZACHARIAH	
ART UNIT	PAPER NUMBER
1648	7

DATE MAILED: 07/30/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/990,909	FALLON, JOAN M.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *28 June 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *8-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, and species (a) in Paper No. 6 is acknowledged. The traversal is on the ground(s) that there is no serious burden on the examiner in examining claims both to a method of detecting biological markers, and to biological markers for specific pathological organisms. This is not found persuasive because examination of the generic method, or of the elected method, does not require a search for any of the specifically claimed biological markers. Further, the search for any one of the claimed biological markers will not be coextensive with the search for any other of the biological markers. Thus, there is a burden on the examiner in examining all of the claimed inventions in a single application.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the claimed methods to the extent that the correlation of the disorder to the pathogen are allegorical, does not reasonably provide enablement for the claimed methods to the extent that the correlations are predictive of the disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to

practice the invention commensurate in scope with these claims. Claim 1 describes a method of determining if an individual has, or may develop, a disease or disorder comprising the steps of

1) obtaining a stool sample from the individual,

2) analyzing the sample to determine the presence of an antigen, and

3) correlating the presence of the pathogen with the disorder, or a lack thereof.

Claims 2-5 each further limit the method of claim 1 to a method wherein the detected pathogen is correlated to one of PDD, dysautonomia, Parkinson's disease, or a neurological disorder (the claimed disorders).

The present claims are not enabled for several reasons. First, the claims are excessively broad in relation to the specification. Secondly, the applicant is not enabled for the claimed method in relation any of the claimed disorders. Finally, the applicant is not enabled for the method wherein the pathogen supposedly predictive of the claimed disorders is H. pylori.

The first ground for rejection is that the claims exceed the scope of the disclosure. A claim is commensurate in scope with the enablement when the applicant has provided sufficient disclosure to enable one skilled in the art to practice the claimed invention without undue experimentation. In re Wands, 8 USPQ2d 1400, 1404 (CAFC 1988). There must be a "reasonable correlation" between the scope of enablement and the scope of the claims. In re Fisher, 166 U.S.P.Q. 18, 24 (CCPA 1970). In the present case, this correlation requires that "there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and how to use the invention as broadly as it is claimed. This means that the disclosure must adequately guide the art worker to determine, without undue experimentation, which species among all those encompassed by the claimed genus possess the

disclosed utility." See, In re Vaeck, 20 U.S.P.Q.2d 1438, 1444 (CAFC 1991) (explaining why disclosure of one working examples in an unpredictable art was insufficient to enable claims to a generic claim covering bacteria from many different genera). Therefore, although neither working examples, nor an explanation of how the invention work are required, they are factors that may be considered when determining the scope of enablement provided by the applicant.

Claim 1 reads on a method for the detection of any disease or disorder by assaying a stool sample for the presence of a particular pathogen. The applicant is not enabled for the full breadth of this claim because the applicant has not indicated which diseases may be correlated with what pathogens, or how to detect the presence of all potential pathogens. The level of experimentation required for this claim is extremely large. The disclosure names six potential pathogens, and four diseases. The applicant has given no guidance beyond these disclosures as to what pathogens are likely to be associated with which disorders. Given that finding pathogens and antigens that are either causative or indicative of diseases is a common pursuit in relation to any disease, and can take years of study, the amount of experimentation required for one of ordinary skill in the art to practice the full extent of this claim is undue. The applicant would have to identify pathogens for most if not every potential disease and disorder to be enabled for this claim.

Secondly, the applicant has not shown that the detection of a pathogen in a stool sample is predictive of any of the claimed disorders. For example, although the art has noted that Helicobacter pylori has been associated with neurological diseases (see, Tsang, HKMJ, 5:169-174); neither the art nor the applicant has shown that indications of H. pylori in a stool sample would lead one in the art to believe that every person so infected either has, or is going to develop, a neurological disease. See e.g., Dobbs et al, Medical Hypothesis 55:93-98, at 96

(indicating that while H. pylori infections may be causative for some instances of Parkinson's disease, Parkinson's is not universally associated with the infection). In order for the applicant to enable such a claim, the applicant must show not just a correlation between the pathogen and the disease in general, but a correlation between a pathogen, and the development of the disease. This is because correlations can exist in the absence of any real predictive relationship. See e.g. Woodward et al., Gut 43:285-287 (indicating a correlation between Clostridium difficile and dysautonomia in that the infection was tested for, but not indicating that the infection has any predictive or causative relation to dysautonomia). In short, the applicant must show that the correlation between those who test positive for the pathogen, and those who have the claimed disorder is not merely allegorical, but has real potential as a diagnostic tool.

In the specification, the applicant does show that individuals with the claimed disorders tend to have infections by multiple pathogens. See, specification, pp. 11-13. However, the applicant has not shown that these infections have a causal relationship with any of the identified diseases. The children tested all already had the disorders. The applicant did not show that children with the disclosed infection were likely to develop the disorder. In order to do so, the applicant would need to show that a percentage of people with the disclosed infections were more likely to develop the diseases than those not infected. The applicant has not shown the percentage of people with infections have developed the disclosed diseases or disorders. Rather, the applicant has only shown that those with the disclosed disorders are more likely than healthy persons to have multiple infections, but have not shown that any one infection is likely to indicate one of the claimed disorders. This is true both for the generic claim, and for the elected pathogen of claim 7, Helicobacter pylori.

With respect to claims wherein the pathogen tested for is H. pylori, the applicant has not shown that the presence of this particular pathogen is necessarily indicative of the claimed disorders, although the bacterium is known to cause other diseases. See, 103 rejection below. However, the applicant has indicated only four diseases for which H. pylori might be a diagnostic tool. Having disclosed only those four diseases, the applicant has not enabled one in the art to practice the claimed method (in this case, the method of claim 7) to the full extent of the claim. This is because the practitioner must discover all of the diseases with which H. pylori correlates. Given the large umber of potential diseases, and the fact the applicant has disclosed only a few diseases other than those already know in the art to be causally associated with H. pylori (thereby providing little guidance), a great amount of experimentation must be conducted. Practicing the invention of claim 7 therefore requires an undue amount of experimentation.

Nor has the applicant enabled claims 3-6 to the extent that they read on methods wherein H. pylori is the pathogen detected. This is for the same reasons as described above regarding these claims in general. The applicant has not shown such a correlation between H. pylori and the claimed diseases such that one in the art would accept that any person who shows evidence of H. pylori infection is likely to develop any of the claimed disorders.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by either Parisi et al., Journal of clinical Microbiology, Vol. 33, pp. 1963-65(Parisi); or U.S. Patent Number 5,607,863, issued to Howard M. Chandler (Chandler). Claim 7 is also rejected, as anticipated by Chandler. Claim 1 describes a method of determining if an individual has, or may develop, a disease or disorder comprising the steps of

1) obtaining a stool sample from the individual,

2) analyzing the sample to determine the presence of an antigen, and

3) correlating the presence of the pathogen with the disorder, or a lack thereof.

Claim 2 further requires that the analyses step comprise a stool immunoassay to determine the presence of an antigen associated with a pathogen. Claim 7 specifies that the pathogen detected comprises Helicobacter pylori.

Parisi teaches an immunoassay for an antigen to Cryptosporidium in stool samples. Abstract. The reference teaches that the assay is testing for the presence of Cryptosporidium specific antigens (CSA) that are associated with Cryptosporidium infections. P. 1963. A positive result for the antigen shows the presence of Cryptosporidium in the individual, therefore allowing for the diagnosis of cryptosporidiosis. Id. Thus, the reference teaches a method with all of the elements of the claimed method.

Chandler teaches an assay device for the detection of analytes in a test sample. Abstract. Among the samples that may be tested are fecal samples. See, e.g. col. 24, lines 20-24. The assay may be used to detect the presence of pathogens (col. 2), and the results of the test may be indicative of a disease (e.g. col. 24, lines 20-24). Further, chandler also teaches that among the

pathogens that may be detected are antibodies to the Helicobacter pylori. Col. 2, lines 32-35. Thus, the reference anticipates all of the identified claims.

6. Claims 1, 2, and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent Number 5,527,678, issued to Blaser et al. (Blaser). Claim 1 is described above. Claim 7 requires that the pathogen correlated with the disease is Helicobacter pylori.

Blaser teaches that Helicobacter pylori is associated with gastric disorders. Col. 1, lines 19-50. The reference further teaches methods of detecting the presence of the bacterium using, or testing for, antibodies in a sample (i.e. immunoassays- see Cruse et al, pp. 152-153, defining an immunoassay as a test that measures antigen or antibody), wherein the methods diagnose H. pylori infection, and disposition to other diseases associated with H. pylori infection. Col. 2,lines 37-51, and col. 1, lines 12-17. Among the samples that may be analyzed are blood, saliva, and stool. Col. 17, lines 23-26.

7. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent Number 5,952,178, issued to Lapidus et al. (Lapidus). Claim 1 is described above. Lapidus teaches a method of analyzing stool samples to diagnose diseases. Col. 1, lines 10-18. The method includes analysis for diseases caused by bacteria, and involves analyzing the stool samples "to detect debris indicative of disease." Col. 1, lines 21-25, and col. 2, lines 51-55.

8. Claim 4 is rejected under 35 U.S.C. 102(b) as being anticipated by Woodward et al., Gut 43: 285-287 (Woodward). Claim 4 read son the method of claim 1, wherein the disorder is a dysautonomic disorder.

The authors of Woodward stated that in the investigations that they performed to determine the cause of the dysautonomia suffered by the subject, they tested for the presence of

Clostridium difficile. Thus, the reference inherently teaches of a correlation, though not present in the case at hand, between a pathogen, and dysautonomic disorders. Further, the analysis conducted comprised of tests on stool samples from the subject. The stool samples were tested for indicia of the presence of C. difficile. Therefore, the reference teaches all of the elements of the rejected claims.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 5 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Parisi or Chandler in view of Dobbs et al, Medical Hypothesis, Vol. 55, pp. 93-98 (Dobbs). Claim 5 describes a method of detecting a pathogen-associated antigen for Parkinson's disease, wherein the pathogen is Helicobacter pylori. The teachings of Chandler and Parisi are described above.

Dobbs teaches that there is a connection between Helicobacter pylori and some forms of Parkinson's disease. P. 96. The reference also suggests that strain typing and serum antibody profiling for H. pylori may result in an "antigen discriminant for parkinsonism," thereby indicating that such an antigen may be correlated with Parkinson's disease. The reference does not indicate that such an antigen may be found through stool sample analysis.

However, when Dobbs is read in view of Chandler or Parisi, it would have been obvious to one of ordinary skill in the art to screen for such an antigen in stool samples. Because H. pylori is generally associated with the gastrointestinal tract, it would have been obvious to one of ordinary skill in the art to identify the antigens suggested by Dobbs in a stool sample, such that assays such a those taught by Chandler and Parisi could be used to help diagnose Parkinson's disease. Assuming that such an antigen could be found, one of ordinary skill in the art would have had a reasonable expectation that the described method would have worked because H. pylori has previously been known to be identifiable by stool assays. See, e.g. Blaser, col. 17, lines 23-26.

11. Claims 1, 6, and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blaser in view of Tsang et al., Hong Kong Medical Journal, Vol. 5, pp. 169-174 (Tsang). Claim 1 is described above. Claim 6 describes a method of detecting a pathogen-associated antigen for a neurological disorder. Claim 7 describes the method of claim 1 wherein the pathogen is Helicobacter pylori. The teachings of Blaser are described above.

Tsang teaches that Helicobacter pylori is known to be causally associated with several diseases (p. 169, col. 1) and seropositively associated with neurological disorders (abstract). However, the reference does not teach a method of analyzing stool samples to detect the presence of the pathogen.

Blaser teaches that the methods of detecting H. pylori disclosed therein may be used in the diagnosis could be used in the diagnosis or the disposition to diseases associated with H. pylori infection (col. 1, lines 13-16). Therefore, it would have been obvious to one of ordinary skill in the art to combine the references to use the methods of detecting H. pylori disclosed by

Blaser to diagnose or determine the disposition of an individual towards the diseases with which Tsang discloses H. pylori is associated, including the neurological diseases. As H. pylori is known to be associated with neurological disorders, and as no change is being made to the methods of Blaser, there would be a reasonable expectation of success in using the Blaser methods to correlate H. pylori and a neurological disease.

12. Claims 3 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Blazer in view of U.S. Patent Number 6,020,310, issued to Beck et al. (Beck). Claim 3 describes the method of claim 1 wherein the disorder is a PDD. Claim 7 and the teachings of Blaser are described above.

Beck teaches methods of diagnosis for autism, a pervasive developmental disorder. Col. 1, lines 13-23. In disclosure of the patent, the reference teaches that "a significant portion of patients with autistic behavior also suffer from mild gastrointestinal symptoms." The reference further indicates that among the tests run in determining the cause of autism, "the gastric biopsies were stained with Giemsa to identify Helicobacter pylori infection." Col. 10, lines 53-58. the reference thus teaches a correlation between the pathogen H. pylori and autism (a PDD). However, the reference does not teach a method of testing for the pathogen by analyzing a stool sample.

Blaser teaches that the methods of detecting H. pylori disclosed therein may be used in the diagnosis could be used in the diagnosis or the disposition to diseases associated with H. pylori infection (col. 1, lines 13-16). Therefore, it would have been obvious to one of ordinary skill in the art to combine the references to use the methods of detecting H. pylori disclosed by Blaser to diagnose or determine the disposition of an individual towards the autism as disclosed

by Beck. As H. pylori is known to be associated with PDDs, and as no change is being made to the methods of Blaser, there would be a reasonable expectation of success in using the Blaser methods to correlate H. pylori and a neurological disease.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 703-308-4240. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Z. Lucas
Patent Examiner
July 29, 2002

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